

FUNDAMENTAL STUDIES OF NEURAL STIMULATING ELECTRODES

**Third Quarterly Report
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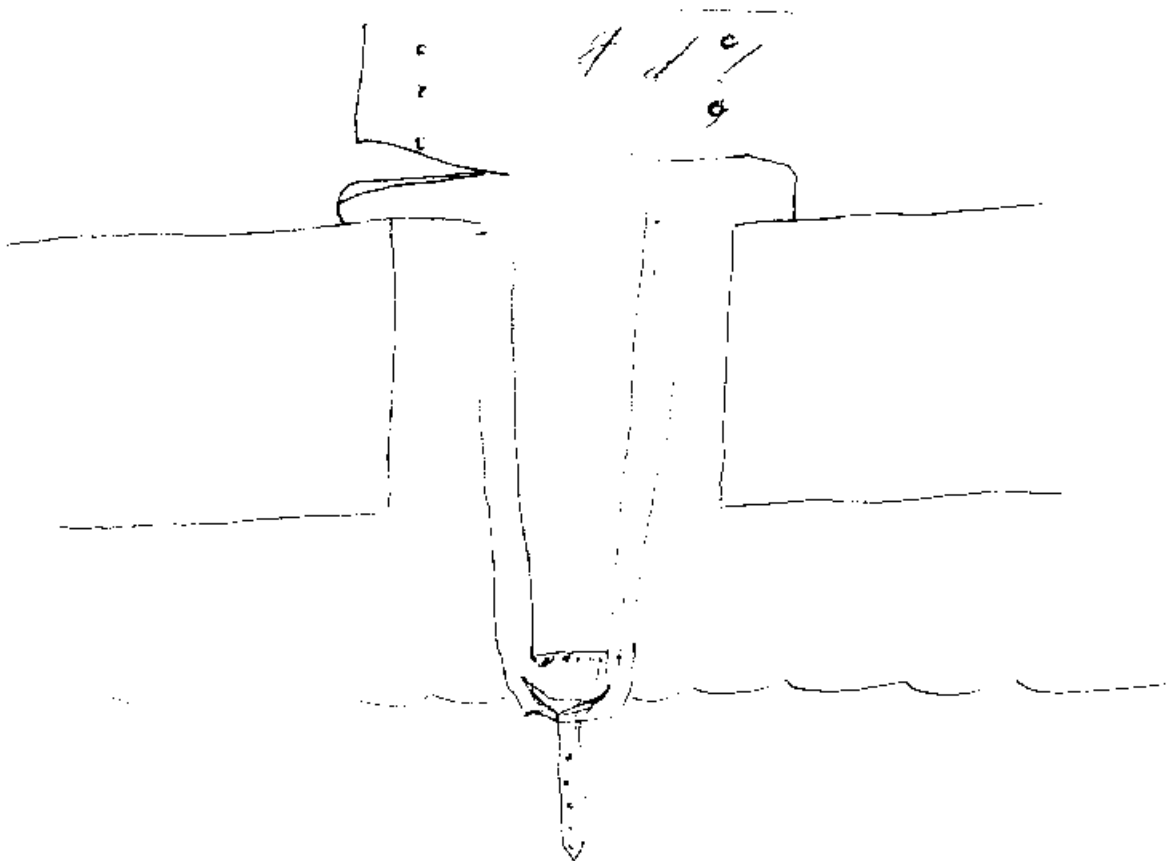
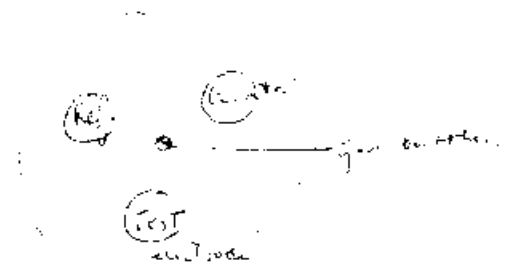
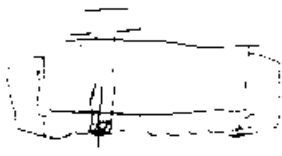


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1.0 INTRODUCTION AND SUMMARY

This report describes the work on NINDS Contract No. N01-NS-4-2310 during the period March 1 to May 28, 1995. As part of the Neural Prosthesis Program, the broad objectives of the present fundamental studies are: 1) to evaluate the electrochemical processes that occur at the electrode-electrolyte interface during pulsing regimens characteristic of neural prosthetic applications; 2) to establish charge injection limits of stimulation electrode materials which avoid irreversible electrochemical reactions; 3) to develop an *in vitro* method, which can be applied *in vivo*, for determining the electrochemical real area and stability of microelectrodes; 4) to develop new materials which can operate at high stimulation charge densities for microstimulation; and 5) to provide electrochemical and analytical support for other research activities in the Neural Prosthesis Program at NINDS.

Electrochemical studies of Ir microelectrodes from U. Michigan and Laboratory for Neural Control, NINDS were continued this quarter. Results obtained from cyclic voltammetry of sites on the U. Michigan probe indicated a continuing degradation of the electrochemical integrity of each site which was initially reported in the last quarterly report. Measurements of the impedance magnitude at 1 kHz do not provide evidence of the changes in electrochemical properties observed by cyclic voltammetry. The phase angle data at 1 kHz suggest the occurrence of a change in properties but the measurement at a single frequency does not provide sufficient information to determine the severity of degradation. A single site was subjected to a standard pulse activation protocol to form AIROL while observing the site color changes with video microscopy. All of the sites showed the color changes associated with oxidation and reduction of the oxide film, even though only one site was actually connected to the potentiostat. This observation confirmed the suspicion raised in the previous quarter that the sites had become electrically continuous, however the mechanism of the electrical connection is still unknown.

Impedance spectroscopy data were analyzed with a curve fitting program to fit the data to an equivalent circuit which might be used to identify elements that are most susceptible to change during prolonged soaking. This analysis is still in a preliminary stage, but a circuit was derived to which a good fit was obtained for data obtained for site #1. Analysis of the data for the remaining four sites is in progress and results will be presented in the next report. The fitting

of the impedance data to an equivalent circuit and monitoring changes in circuit elements over time of soaking appears promising for identifying changes in an electrode site during soaking. However, at the present time, interpretation of the circuit element changes is best done in conjunction with cyclic voltammetry for qualitative diagnosis of changes in electrode properties.

2.0 Ir MICROELECTRODE STUDIES

Ongoing studies of Ir microelectrodes are concerned with identifying method(s) which would be useful for *in vivo* monitoring of microelectrode stability and characterization of their electrochemically active surface area. The test electrodes have been soaking in PBS for several months with cyclic voltammetry in PBS or in Ru hexamine solution, and impedance spectroscopy performed intermittently. The electrodes being evaluated in these long term studies were described in the previous report and are the following:

1. Michigan probe CN8-49 with five sputtered Ir sites numbered 1-5; each site was designed with a geom. surface area of $800\text{ }\mu\text{m}^2$.
2. Dual hatpin Ir microelectrodes from M. Bak, NINDS, identified as BAK-11A and BAK-11B.

Data are presented in this report only for Michigan probe CN8-49. Results on BAK-11A and 11B will be updated in the next quarterly report.

Experimental Methods

The experimental methods employed in these long term studies were described in the previous report. Solutions were changed by using a syringe equipped with flexible tubing to extract solution from the cell, and to replenish the cell with new solution. When changing from Ru solutions to PBS, or *vice versa*, the cell was flushed several times with the incoming solution. We elected to use room temperature PBS for this soak test because it does not require a continuous stream of CO_2 as does the Earle's balanced salt solution used in prior long term soak tests of macro-sized electrodes. The electrochemical cell employed with the microelectrodes is not well suited for 37°C testing with continuous gas bubbling over a prolonged period of soaking because of its small volume and the increased possibility of losing water from the solution due to evaporation.

The protocol for testing site stability during the past quarter involved acquiring periodic cyclic voltammograms (CVs) of all sites in the PBS soak solution at scan rates of 0.05, 10, 20, 50, 100 and 200 V/sec. In addition to these intermittent CVs in PBS, scan rate study No. 3 was

performed in Ru hexaammine-PBS solution and in PBS. In this scan rate study, CVs were acquired at scan rates ranging from 0.001 to 200 V/s as described previously.

Impedance spectra were acquired over a frequency range of 10^{-1} Hz to 10^5 Hz for all sites at various times during the soaking period. Impedance data were analyzed with an equivalent circuit fitting program (Equivalent Circuit, by Bernard A. Boukamp, Univ. of Twente, 1989).

Light microscopic examination of sites on the probe during electrochemical activation was performed with a Sony Video Camera attachment with real time recording of site responses to electrochemical activation protocol.

Results and Discussion

Cyclic Voltammetry

Figure 2.1 shows CVs acquired at site 1 in the storage PBS electrolyte at different times during this quarter. On day 61, a CV was acquired first in aerated PBS. This CV has a non-zero current at the start of the scan, is slanted diagonally, and shows a large increase in cathodic current as the scan progresses from 0 V to -0.4 V. After the solution was deaerated the CV showed an even higher overall current (note the change in current scale), had a higher initial current at the beginning of the scan, and was skewed diagonally. A CV acquired on day 79 showed an increase in current and similar diagonal orientation about the current axis. The CV acquired on day 85 showed a lower overall current and is less skewed in the potential range between 0.1V to -0.2V, but has cathodic and anodic current peaks which may be due to reactions of surface contaminant(s) or of some other component of the probe which has come into contact with the electrolyte. Although CVs are illustrated in Figure 2.1 only for site 1 on CN8-49, nearly identical CVs were obtained at the other four sites on each day of testing after day 20, including the abnormal CV on day 85.

On day 62 a Ru hexaammine scan rate study was performed even though the CVs in PBS showed significant degradation of site integrity. We hoped that usable data might be obtained with which electrochemical surface area numbers could be determined. Figure 2.2 compares CVs acquired at 50 mV/sec in Ru-PBS solution and in the PBS supporting electrolyte in the day 62 scan rate study with similar sets of CVs from scan rate studies on days 2 and 20. The CV taken in Ru solution on day 62 shows a faradaic current for the reduction reaction at site 1 that is approximately the same as that observed on day 20. The CV in Ru solution does not show the

severe distortion and high current seen in the background CVs acquired in PBS on either days 61 or 62. This would suggest that some component(s) may be contributing to the background current in PBS which do not participate in the faradaic process in Ru solution. The distortion of the CVs in PBS made it impossible to perform the usual analysis of scan rate data to estimate site dimensions.

An additional abnormality of the CVs in PBS was a large anodic current at the initial potential of 0.1 V vs Ag/AgCl. Normally there should be zero current in PBS at this potential. The substantial anodic current indicates an atypical condition, but the reason for it was not clear at the time the CVs were obtained. However, when impedance measurements were taken on day 83, the open circuit potential was found to be about 200-300 mV more negative than on day 28, and it is possible that this condition was present on day 62 when the scan rate study was performed. The cathodic shift in open circuit potential might occur if electrolyte penetration resulted in exposure of other components of the probe to the solution. Initiating a CV at a potential more anodic than the open circuit potential could produce the current which was observed at the beginning of the CV in PBS on day 62. In the absence of visual evidence at this time, it is not possible to be more precise about the exact failure mode of this probe. However, it is clear that CVs in the PBS soak solution provided ample evidence of the degradation of electrochemical behavior of the sites on this probe.

In Situ Light Microscopy of Site Activation

The acquisition of video photomicrography instrumentation makes it possible to photograph electrodes *in situ* during electrochemical experiments. As indicated in the previous report, and by the abnormal CV behavior observed in PBS, we suspect that the penetration of electrolyte beneath insulating layers has resulted in electrical contact being established between sites. The mechanism of contact could be via corrosion products or salt precipitates between contact pads on the probe. In order to verify this conclusion, the probe was video taped while one site (site #5) was subjected to an electrochemical activation protocol until color changes were observed at the site indicating the alternating oxidation and reduction reactions of Ir oxide. After about 300 potential cycles, these color changes were observed, not only at the site connected to the potentiostat, but also at all of the other sites, thereby confirming the electrical continuity between sites.

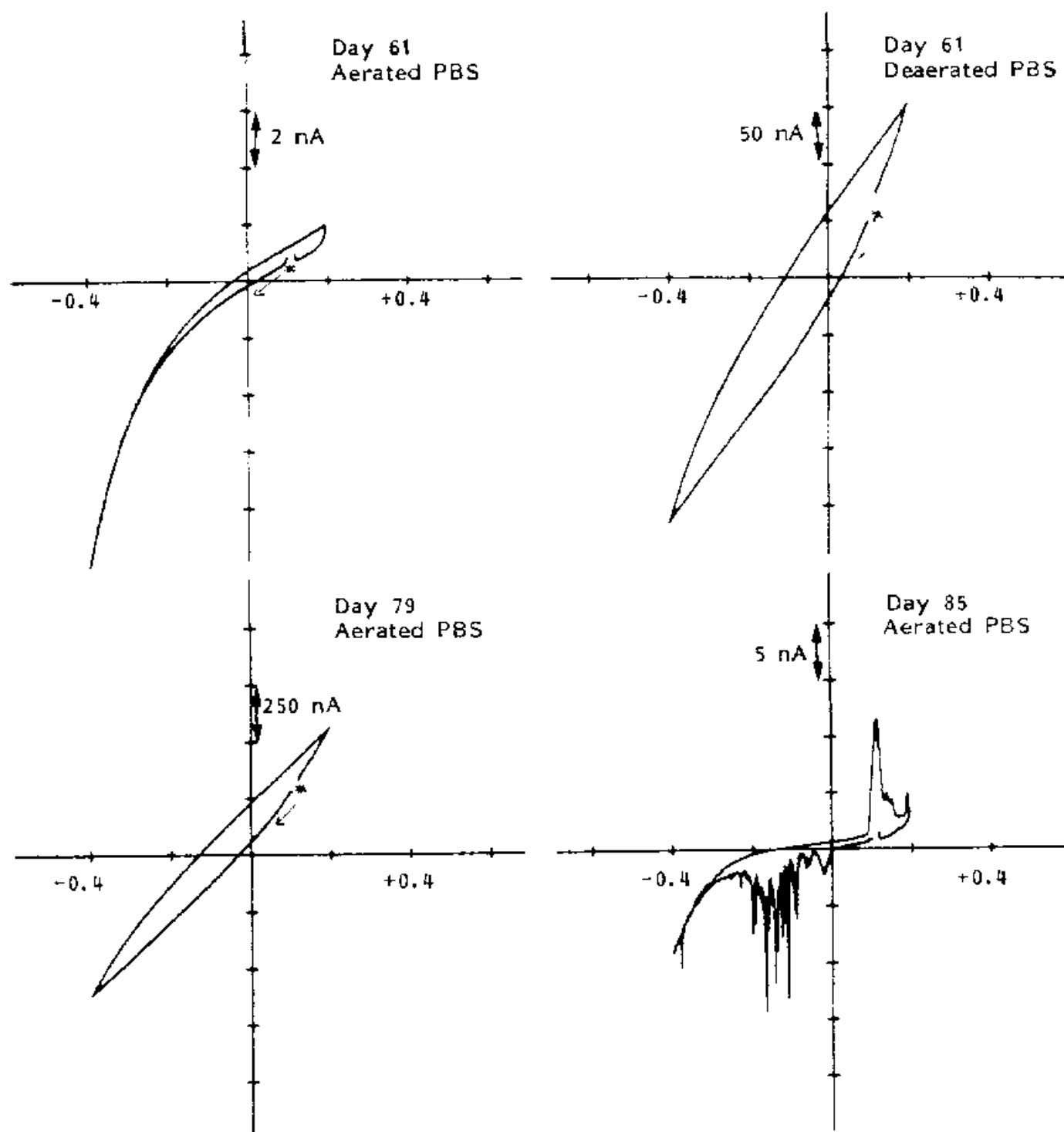


Figure 2.1 Cyclic voltammograms acquired at site 1 on U-Mich. probe CN8-49 on days 61, 79 and 85 in PBS soak solution. Scan rate 0.05 V s⁻¹. Potential scale vs Ag/AgCl.

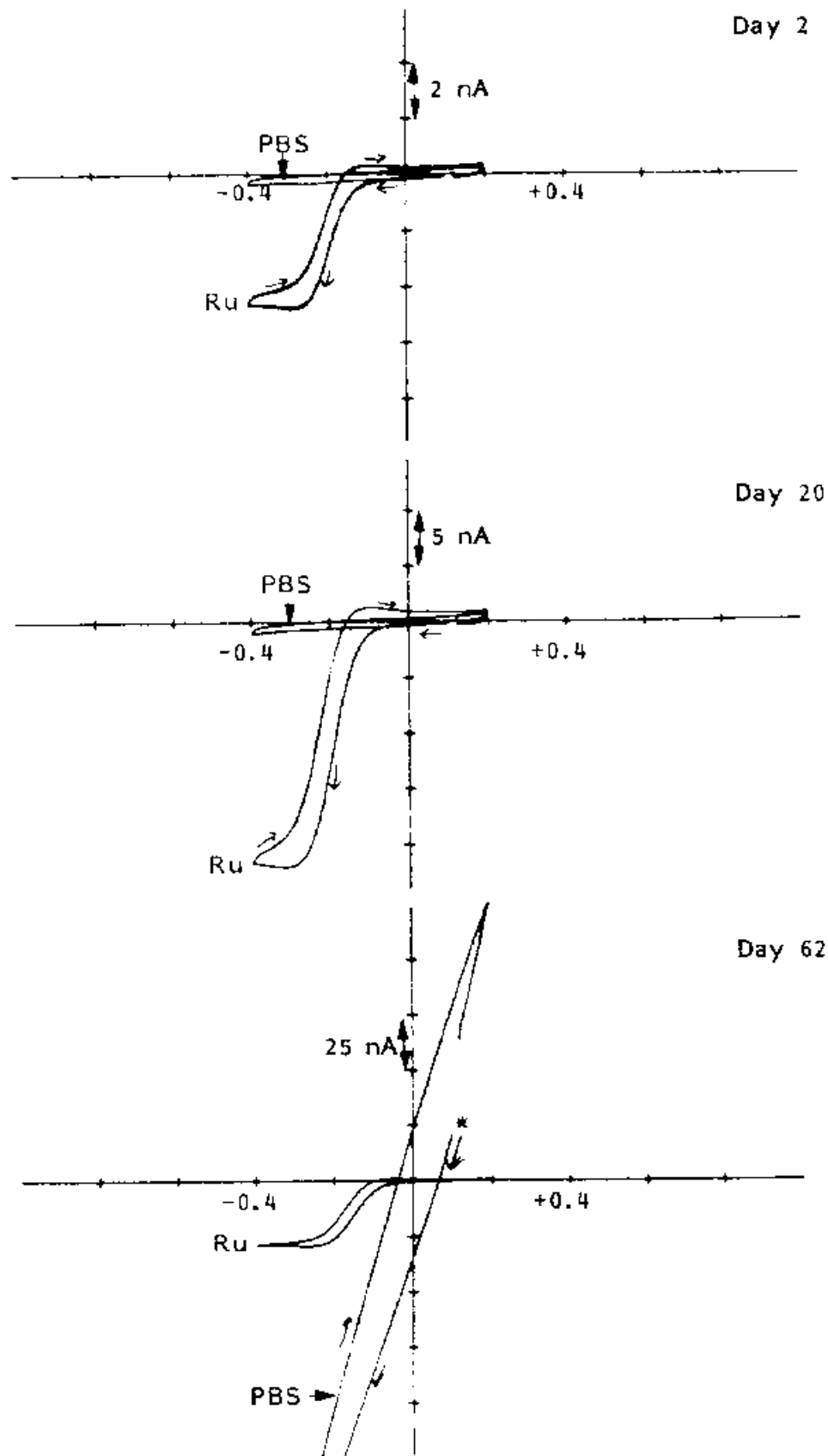


Figure 2.2 Cyclic voltammograms acquired in the solutions indicated at site 1 on U. Michigan probe CN8-49 on days 2, 20 and 62. Scan rate = 0.05 V/s. Potential scale vs. Ag/AgCl. Ru = 1 mM $\text{Ru}(\text{NH}_4)_6\text{Cl}_3$ in PBS. All solutions deaerated. Arrows indicate direction of scan.

Cyclic voltammetry of the sites following the activation protocol showed typical voltammetric curves of activated Ir. Figure 2.3 illustrates a CV acquired at site #1 following activation of site #5. All five sites gave similar CVs. Moreover, joining the leads to all five sites and acquiring a CV from the connected sites gave the same CV as that obtained with connections to individual sites. Note that this CV shows a significant anodic current at the initial potential prior to the scan, similar to that seen on the site before activation.

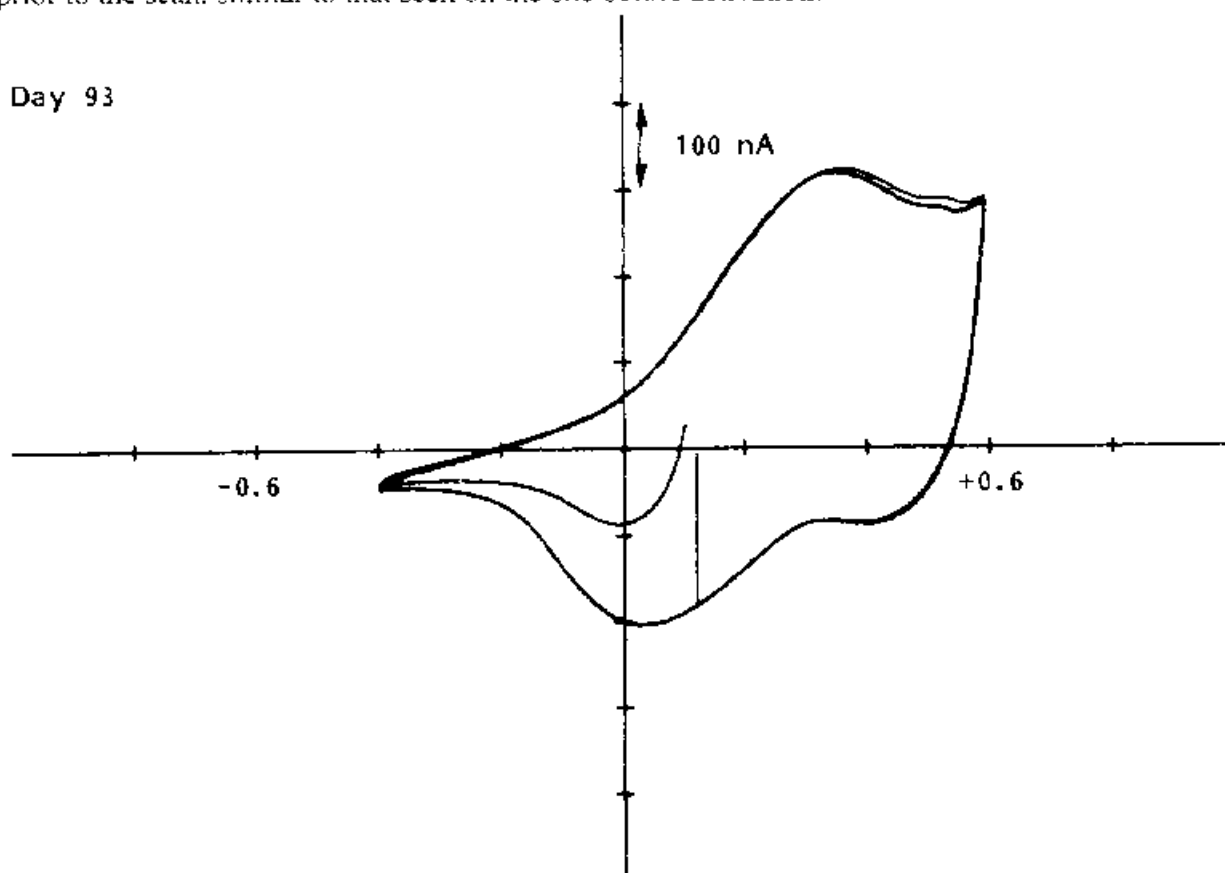


Figure 2.3. Cyclic voltammogram acquired at site 1 on U. Mich. probe CN8-49 on day 93 after pulse activation of site 5. Scan rate = 0.05 V/s. Potential scale = Ag/AgCl.

Impedance Spectroscopy

Table 2.1 lists the impedance magnitudes and phase angles measured at 1 kHz of the 5 sites on probe CN8-49 over the entire period of observation. In the previous report, which covered the data up to 28 days of soaking, we noted that the initial impedances at 1 kHz of the five sites varied, but these decreased and became similar to each other over time. No measurements were made between days 28 and 83, but at day 83 the site impedances had

increased, but still varied only slightly from site to site. On day 83, an impedance measurement was also taken with leads of all five sites banded together. This impedance value was slightly lower than those of the individual sites. After activation of site 5 as part of the video demonstration of continuity between sites, an impedance spectrum was taken of site 1. The magnitude at 1 kHz showed a decrease to 67 k Ω with a phase angle of -23. At this time, an impedance measurement was taken again with leads of the five sites connected together. The magnitude at 1 kHz was 39 k Ω with a phase angle of -23.16. The similarity of the site #1 data and the five site data provides additional evidence for electrical continuity between individual sites.

Table 2.1 Impedance (k Ω) and Phase Angle at 1 kHz of Ir sites on Probe CN8-49.

Time	Conditions during Impedance Measurement	Site 1	Site 2	Site 3	Site 4	Site 5	All Sites
Day 1	PBS $\text{Ru}(\text{NH}_4)_2\text{Cl}_2$ α 100 mV vs Ag/AgCl	494 -76.51	325 -73.87	781 -76.35	399 -73.66	727 -77.84	
Day 8	PBS $\text{Ru}(\text{NH}_4)_2\text{Cl}_2$ α OCP -40 to 100 mV	478 -54.34	281 -62.02	471 -53.29	346 -57.95	532 -47.47	
Day 11	PBS α 100 mV	237 -45.75	192 -60.22	295 -51.15	213 -56.36	243 -46.52	
Day 26	PBS α 100 mV	153 -64.89	155 -65.05	257 -49.86	204 -55.29	159 -61.47	
Day 28	PBS α 100 mV	125 -61.79	135 -62.84	165 -60.11	144 -60.60	130 -62.20	
Day 83	Impedance taken in PBS α OCP: -100 to -120 mV	207 -82.17	212 -81.3	217 -81.26	217 -82.05	216 82.28	188 -82.86
Day 84	Impedance taken in PBS of Site # 4 only α -110 mV	190 -79.51					
Day 85	Impedance taken in PBS of Site # 1 only α -167 mV	118 -36.45					
Day 90	Impedance taken in PBS α OCP: -120 to -145 mV	203 -76.1	221 -71.2	229 -66.69	206 -71.83	208 -74.71	
Day 93	Impedance taken in PBS of Site #1 only α OCP: -180 mV (after activation protocol applied to site 5)	67 -23					39 -23.16

Table 2.1 also shows the open circuit potentials at the time that the impedance measurements were made. From day 83 on, the open circuit potentials were more negative than

is typical of Ir, and much more negative than is to be expected for activated Ir. The values are more like those that were observed for galvanic couples of polysilicon-Al(OH) and polysilicon-Ir [1].

Plots of the entire frequency spectrum of impedance and phase angle at different times during the soaking period are shown in Figure 2.4. These plots demonstrate the similarity in the impedance spectra which developed over time. Whereas the initial spectra showed sites #1 and #2 to be different from sites #3, 4, and 5, by day 90 no such distinction was apparent. The spectrum taken of site #1 on day 85 was completely different from all others taken on any day. The unique impedance behavior may be related to the unique voltammetric curves observed on the same day.

More detailed analysis of the impedance data was initiated this quarter. The data were fitted to an equivalent circuit which we hope might be utilized to identify elements which change during long term soaking. The best fit of the data was obtained with the equivalent circuit shown in Figure 2.5. The values of circuit elements are listed in Table 2.2. The element R_1 is considered to represent the ohmic resistance. Its value fluctuated between 28-40 k Ω over the first 20 days, but then decreased at the longer soaking times. The trend toward lower values of R_1 is consistent with an increase in real exposed surface area, and fluctuations within each group of values, e.g. 0-28 days vs 83-90 days, may reflect changes in contact resistance, intra-site contacts, or electrolyte resistivity. The element C_1 increased from 260 pF to almost 833 pF and might be assigned to the double layer capacitance. It is premature to make assignments for the elements W , C_2 , and R_2 at this time. However it is noteworthy that they had their most different values on day 85, on which day the CVs in PBS displayed the prominent current peaks believed to be due to surface contaminant(s). The impedance data obtained on days 8, 11, and 85 could not be fit to the equivalent circuit without the addition of element R_2 . The assignment of this element to a probe component is not feasible at this time.

The same circuit is being used for the impedance data for the other four sites on the probe. Completion of this task may enable a better correlation of circuit elements with components of the probe, or at least an identification of those elements which are associated with the deterioration of site integrity.

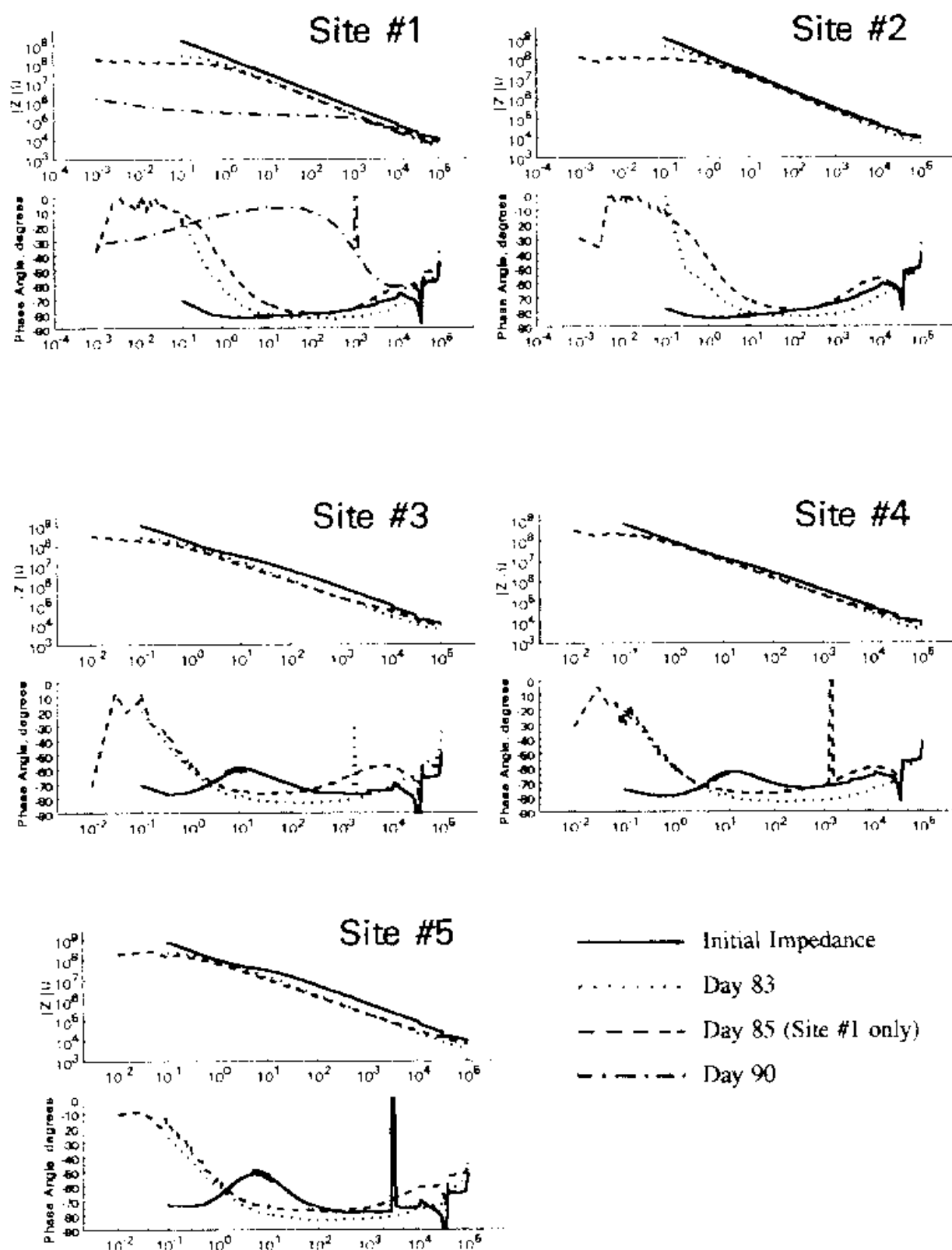


Figure 2.4 Impedance and phase angles of sites on U. Mich. probe CN8-49 at different times of storage.

Table 2.2 Values of circuit elements obtained by fitting impedance data to the equivalent circuit shown in Figure 2.5.

Soak Time (Days)	χ^2 (Model)	R_1 k Ω	C_1 pF	R_2 k Ω	W nMOH	C_2 pF	R_3 M Ω	Circuit Descriptor
1	4.93 E-3	28	260		6	432	4240	$R(C[W(RC)])$
8	2.44 E-3	40	218	550	37	3830	1690	$R(C[RW(RC)])$
11	1.50 E-3	21	265	127	78	3884	1060	"
20	4.77 E-3	20	453		67	1829	2980	$R(C[W(RC)])$
28	2.82 E-3	13	421		96	2896	1030	"
83	4.31 E-3	7	677		9	856	164	"
84	3.35 E-4	8	656		20	786	46	"
85	4.6 E-3	11	833	151	8014	125600	<1	$R(C[RW(RC)])$
90	7.11 E-3	17	592		18	1040	59	$R(C[W(RC)])$



Figure 2.5 Equivalent circuit for site #1 on Mich. probe CN8-49.

Conclusions

The results of all electrochemical measurements made on probe CN8-49 this quarter indicate that the individual sites have lost their isolation and are electrically connected to each other. Of all the measurements taken, the cyclic voltammetry in PBS provided the least ambiguous identification of the deterioration of the probe even though the underlying causes and specifics of the deterioration remain unknown. We had planned to end the soak test to examine the probe microscopically, but prefer at this time to continue with the electrochemical monitoring

since the sites are now activated and we can monitor visually the extent of interconnection between them. The fitting of the impedance data to an equivalent circuit and monitoring changes in circuit elements over time of soaking appears promising for identifying changes in an electrode site during soaking. However, at the present time, interpretation of the circuit element changes is best done in conjunction with cyclic voltammetry for qualitative diagnosis of changes in electrode properties.

3.0 WORK FOR NEXT QUARTER

The analysis of the impedance data collected on sites 2-4 on U. Mich. probe CN8-49 will be completed. Scan rate data obtained during this quarter on BAK-11A and 11B will be analyzed together with impedance data from those electrodes for presentation in the next quarterly progress report. New electrodes will be added to this study as they are received from other contractors.

4.0 REFERENCES

1. Robblee, L. S. et al., Studies of the Electrochemistry of Stimulating Electrodes. Contract No. N01-NS-1-2300. Quarterly Progress Report No. 10, March, 1994; Final Report, August, 1994.